REMARKS

In the Final Action dated March 25, 2003, claims 13-30 are pending. Claims 13-18 and 24-30 are under consideration. Claims 16, 28 and 30 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. Claims 17 and 29 are rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enabling support. Claims 13 and 16 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Sato et al. (*Vet. Microbiol.* 43(2): 173-182, 1995), as evidenced by Petre et al. (U.S. Patent 6,013,264). Claims 13-15 and 24 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Zarkasie et al. (*J. Vet. Med. Sci.* 58: 87-89, 1996), as evidenced by Barenholz et al. (U.S. Patent 6,156,337). Claims 13, 14 and 24 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Groschup et al. (*Epidemiol. Infect.* 107: 637-49, 1991), as evidenced by Barenholz et al. Claims 13, 16, 17 and 25-27 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Zarkasie et al. (*J. Vet. Med. Sci.* 58: 87-9, 1996). Claims 13, 16-18 and 28 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Dayalu et al. (WO 91/18627) in view of Sato et al., Zarkasie et al. and Barenholz et al. Claims 17, 28 and 30 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Dayalu et al. in view of Groschup et al., or Zarkasie et al. and Barenholz et al.

This Response addresses each of the Examiner's rejections. Applicants therefore respectfully submit that the present application is in condition for allowance or at least in better condition for appeal. Favorable consideration of all pending claims is therefore respectfully requested.

Claims 16, 28 and 30 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. Specifically, the Examiner objects to the trade names "Tween 80" and "Span 80", as recited in Claims 28 and 30. In addition, the Examiner objects to the recitation

"...X" in claim 16.

In response, Applicants have amended claims 28 and 30 to replace the recitation "about 5.6% v/v Tween 80 and about 2.4% v/v Span 80" with the recitation "about 8% v/v of an amphiphilic surfactant". Support for such amendment is found in the specification, e.g., at page 4, lines 1-2, and in claim 18. Applicants have also amended claim 16 to recite "fold" in place of "X". As such, it is respectfully submitted that the claims, as amended, are not indefinite. Withdrawal of the rejection under 35 U.S.C. § 112, second paragraph is therefore respectfully requested.

Claims 17 and 29 are rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enabling support. The Examiner admits that the specification is enabling for a vaccine composition comprising about 10-fold concentrated culture filtrate antigen of *E. rhusiopathiae*, produced following formalin or BPL inactivation, and combined with about 30% v/v REHYDRAGEL 10% lecithin in DRAKEOL™ mineral oil, 5.6% Tween 80 and 2.4% Span 80 in PBS, which provided immunity to weaned pigs after storage at 4°C for at least 6 months. However, the Examiner contends that the specification does not reasonably provide enablement for a vaccine composition comprising a concentrated culture fluid fraction of *E. rhusiopathiae* as recited, which contains an adjuvant plus any metal hydroxide, any metal phosphate, a calcium phosphate gel, or zinc hydroxide/calcium hydroxide gel as a stabilizing agent at any concentration, that is stable for at least one year and that provides immunity to weaned pigs for six months.

In response, Applicants respectfully submitted that claim 17 has been amended to incorporate the recitations of claim 18 to further characterize the adjuvant component of the vaccine composition. Claim 18 is therefore canceled without prejudice. Applicants further

submit that claim 29 has been canceled without prejudice. New claim 31 depends from claim 30 and is supported by previously presented claim 29. Applicants respectfully submit that claims 17 and 31, as amended, are fully supported by an enabling disclosure. As such, withdrawal of the rejection of claims 17 and 29 under 35 U.S.C. §112, first paragraph, is respectfully requested.

Claims 13 and 16 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Sato et al. (*Vet. Microbiol.* 43(2): 173-182, 1995), as evidenced by Petre et al. (U.S. Patent 6,013,264).

Sato et al. disclose the preparation of filtrate fractions from the culture supernatant of *E. rhusiopathiae*. Each fraction was fixed with aluminum phosphate gels for the preparation of an immunogen, which was injected subcutaneously into mice.

Applicants previously submitted that the term "aluminum phosphate" has been deleted from claim 13, and claim 17 has been amended to include a stabilizing agent as a part of the vaccine. Applicants argued that Sato et al. describe aluminum phosphate to be an adjuvant and that the vaccine of Sato et al. does not include a stabilizing agent. Applicants also argued that Sato et al. do not teach any antigen composition that is stabilized for at least one year at 2°C to 8°C and that provides immunity to weaned pigs for six months.

The Examiner now argues that claims 13 and 16 do not include the limitation that the composition is stable for at least one year at 2 to 8°C and that it elicits immunity to weaned pigs for six months. The Examiner also argues that the antigenic composition of claim 13 is still anticipated by Sato et al. because Sato's aluminum phosphate meets the claim limitation "metal phosphate". With regard to claim 16, the Examiner contends that the recited concentration is considered as an inherent part of the antigen concentration obtained by ultrafiltration in Sato et al., absent evidence to the contrary.

In an effort to favorably advance the prosecution of the present application, Applicants have amended claim 13 to incorporate the recitations of claim 14, i.e., to recite that the *E. rhusiopathiae* culture is inactivated. Claim 14 is canceled without prejudice in light of the amendment to claim 13. Applicants further submit that Sato et al. do not teach an antigenic composition containing an *E. rhusiopathiae* culture fluid fraction that is inactivated. Thus, Applicants respectfully submit that the antigenic compositions of claims 13 and 16 are not taught by Sato et al. Withdrawal of the rejection of claims 13 and 16 under 35 U.S.C. §102(b) based on Sato et al. is therefore respectfully requested.

Claims 13-15 and 24 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Zarkasie et al. (*J. Vet. Med. Sci.* 58: 87-89, 1996), as evidenced by Barenholz et al. (U.S. Patent 6,156,337).

In response, Applicants have amended independent claim 13 to further delineate the *E. rhusiopathiae* culture liquid fraction to be "substantially free of cells of *E. rhusiopathiae*". Support for this amendment is found in the specification, e.g., at page 4, line 34 to page 5, line 12. Zarkasie et al. teach a composition prepared from a whole broth culture of *E. rhusiopathiae* (i.e., containing both a culture fluid fraction and cells of *E. rhusiopathiae*) and aluminum hydroxide gel. Zarkasie et al. do not teach an antigenic composition containing a culture filtrate that is substantially free of cells of *E. rhusiopathiae*. Therefore, Zarkasie et al. do not teach the antigenic compositions, as presently claimed. As such, the rejection of claims 13-15 and 24 under 35 U.S.C. §102(b) based on Zarkasie et al. is overcome. Withdrawal of the rejection is therefore respectfully requested.

Claims 13, 14 and 24 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Groschup et al. (*Epidemiol. Infect.* 107: 637-49, 1991), as evidenced by Barenholz et al.

The Examiner alleges that Groschup et al. teach an antigenic or vaccine composition comprising a culture supernatant antigen of *E. rhusiopathiae*, obtained from inactivated *E. rhusiopathiae*, which protected mice against E. *rhusiopathiae* infection challenge and which reacted with sera from pigs convalescing from *E. rhusiopathiae* infection.

Applicants respectfully submit that contrary to the Examiner's allegation, Groschup et al. do not teach an antigenic or vaccine composition comprising a culture supernatant of *E. rhusiopathiae* that is inactivated. Applicants respectfully submit that independent claim 13, as presently amended, recites that the *E. rhusiopathiae* culture is inactivated, and that claim 14 has been canceled. As such, it is respectfully submitted that the antigenic compositions of claims 13 and 24, as amended, are not taught by Groschup et al. Withdrawal of the rejection under 35 U.S.C. §102(b) based on Groschup et al. is respectfully requested.

Claims 13, 16, 17 and 25-27 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Zarkasie et al. (*J. Vet. Med. Sci.* 58: 87-9, 1996).

The Examiner admits that Zarkasie et al. do not disclose the additional presence of an adjuvant in their composition, or the final concentration of aluminum hydroxide to be 30% v/v. However, the Examiner contends that adding an art-known adjuvant to an art-disclosed microbial vaccine was well known and routinely practiced in the art at the time of the instant invention for the purpose of further enhancing the immunogenicity of a vaccine. The Examiner also contends that the optimization of concentration of aluminum hydroxide or fluid antigenic fraction is well within the realm of routine experimentation.

Applicants respectfully submit that claims 13 and 17, as amended, are directed to an antigenic composition and a vaccine composition, respectively, which contain a culture liquid fraction of *E. rhusiopathiae* that is substantially free of cells of *E. rhusiopathiae*. Applicants

respectfully submit that Zarkasie et al. merely teach a composition prepared from a whole broth culture of *E. rhusiopathiae* (i.e., containing both culture fluid fraction and cells of *E. rhusiopathiae*) and aluminum hydroxide gel. Zarkasie et al. do not teach or suggest making a culture filtrate that is substantially free of *E. rhusiopathiae* cells. Accordingly, it is respectfully submitted that the antigenic compositions and vaccine compositions, as presently claimed, are not rendered obvious by Zarkasie et al. Withdrawal of the rejection of claims 13, 16, 17 and 25-27 under 35 U.S.C. §103(a) in view of Zarkasie et al. is therefore respectfully requested.

Claims 13, 16-18 and 28 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Dayalu et al. (WO 91/18627) in view of Sato et al., Zarkasie et al. and Barenholz et al.

According to the Examiner, Dayalu et al. disclose a vaccine composition comprising an *Erysipelothrix rhusiopathiae* antigen extract and aluminum hydroxide. The Examiner admits that Dayalu et al. are silent about whether or not the antigen extract is a fluid fraction from an *Erysipelothrix rhusiopoathiae* culture. However, the Examiner argues that Sato et al. disclose an antigenic composition comprising a culture filtrate antigen of an *Erysipelothrix rhusiopathiae* culture, and that Zarkasie et al. disclose a fluid antigenic fraction of *Erysipelothrix rhusiopathiae*. According to the Examiner, Zarkasie et al. further teach that protective antigens of *Erysipelothrix rhusiopathiae* are abundant in the culture supernatant. The Examiner contends that it would have been obvious to one of ordinary skill in the art, at the time the invention was made, to replace the *Erysipelothrix rhusiopathiae* antigen extract in Dayalu's vaccine composition with Sato's culture filtrate antigen of *Erysipelothrix rhusiopathiae* culture to produce the vaccine composition of the instant invention, with a reasonable expectation of success. The Examiner contends that one skilled in the art would have been motivated to produce the instant invention for the expected

benefit of providing a vaccine composition that comprises protective antigens of *Erysipelothrix rhusiopathiae*, because culture filtrate antigens were known in the art to serve as protective antigens, as taught by Zarkasie et al.

Applicants respectfully submit that independent claims 13 and 17, as amended recited, are directed to an antigenic composition and a vaccine composition, respectively, which contain a liquid fraction of an *E. rhusiopathiae* culture that is inactivated. None of Dayalu et al., Sato et al., Zarkasie et al. or Barenholz et al. teach or suggest making an antigenic or vaccine composition with a liquid fraction of an *E. rhusiopathiae* culture that is inactivated. None of these cited references provided any motivation for those skilled in the art to inactivate an *E. rhusiopathiae* culture for preparing an antigenic or vaccine composition. In fact, inactivation could reduce the antigenicity of an *E. rhusiopathiae* culture, as described in the present specification, at page 11, lines 29-31, for example. Therefore, it is respectfully submitted that Dayalu et al., Sato et al., Zarkasie et al. and Barenholz et al., taken individually or in combination, do not teach or suggest the antigenic compositions or the vaccine compositions, as presently claimed. Accordingly, the rejection of the claims under 35 U.S.C. §103(a) based on the combination of Dayalu et al., Sato et al., Zarkasie et al. and Barenholz et al., is overcome. Withdrawal of the rejection is therefore respectfully submitted.

Claims 17, 28 and 30 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Dayalu et al. in view of Groschup et al., Zarkasie et al. and Barenholz et al.

The Examiner admits that Dayalu et al. are silent about whether or not the antigen extract is a fluid fraction from the *Erysipelothrix rhusiopathiae* culture, and that Dayalu et al. do not disclose the specific concentrations of the adjuvant recited in the claims. However, the Examiner argues that Zarkasie et al. and Groschup et al. each disclose a fluid antigenic fraction

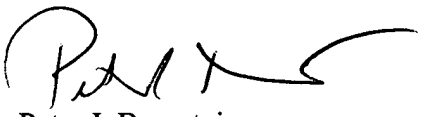
of *Erysipelothrix rhusiopathiae*. The Examiner contends that it would have been obvious to one of ordinary skill in the art, at the time the invention was made, to replace the *Erysipelothrix rhusiopathiae* antigen extract in Dayalu's vaccine compostion with Groschup's or Zarkasie's culture filtrate antigen of *Erysipelothrix rhusiopathiae* culture to produce the vaccine composition of the instant invention, with a reasonable expectation of success. According to the Examiner, one skilled in the art would have been motivated to produce the instant invention for the expected benefit of providing a vaccine composition that comprises protective antigens of *Erysipelothrix rhusiopathiae*, because culture filtrate antigens were known in the art to serve as protective antigens, as taught by Zarkasie et al.

Applicants respectfully submit that independent claims 17 and 30, as presently recited, are directed vaccine compositions which contain a liquid fraction of an *E. rhusiopathiae* culture, wherein the culture is inactivated and the liquid fraction is substantially free of *E. rhusiopathiae* cells. As the Examiner has admitted, Dayalu et al. do not teach a composition containing a fluid fraction from the *Erysipelothrix rhusiopathiae* culture. Zarkasie et al. merely teach a composition prepared from a whole broth culture of *E. rhusiopathiae* and aluminum hydroxide gel. Zarkasie et al. do not teach or suggest making a culture filtrate that is substantially free of *E. rhusiopathiae* cells. Furthermore, Groschup et al. do not teach an antigenic or vaccine composition comprising a culture supernatant of *E. rhusiopathiae* that is inactivated. Thus, the cited references, taken individually or in combination, do not teach or suggest a vaccine composition containing a liquid fraction of an *E. rhusiopathiae* culture, wherein the culture is inactivated and the liquid fraction is substantially free of *E. rhusiopathiae* cells, as presently claimed. None of the cited references provided any motivation for those skilled in the art to try to make the presently claimed composition.

Accordingly, it is respectfully submitted that the rejection of under 35 U.S.C. §103(a) based on Dayalu et al. in view of Groschup et al., Zarkasie et al. and Barenholz et al., is overcome. Withdrawal of the rejection is therefore respectfully requested.

In view of the foregoing amendments and remarks, it is respectfully submitted that the present application is condition for allowance, which action is earnestly solicited.

Respectfully submitted,



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